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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/002,634	12/05/2001	Anthony E. Bolton	033136-226	1971

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EXAMINER	
BELYAVSKYI, MICHAIL A	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 02/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/002,634	BOLTON ET AL.	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-11 are pending.

1. Applicant's election with traverse of Group III, claims 1-10 in Response to Restriction Requirement, filed on 11/21/03 is acknowledged. Applicant traverse the Restriction Requirement on the grounds that the inventions must be both independent and distinct and an undue search burden on the examiner. However, MPEP 803 states that the Inventions be either independent or distinct and a burden on the Examiner if restriction is required.

Regarding applicant's comments about undue burden, the MPEP 803 (August 2001) states that "For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification separate status in the art, or a different field of search". The Restriction Requirement enunciated in the previous Office Action meets this criteria, indicates that inventions recognized divergent subject matter and that a different field of search would be required based upon the structurally distinct products recited and the various methods of use comprising distinct method steps. Moreover, a prior art search also requires a literature search. All the above establishes that serious burden is placed on the examiner by the examination of more than one Group. The Inventions are distinct for reasons elaborated in the previous Office Action and above.

The requirement is still deemed proper and is therefore made FINAL.

Upon further consideration the prior art search has been extended to include Claim 11, as it reads on a process of decreasing the expression of one or more of the inflammatory cytokines IFN $-\gamma$ and IL-6 from cells in a mammalian , comprising administering stressed mammalian blood cells wherein stressor is oxidative conditions and ultraviolet radiation

Claims 1-11 drawn to a method of treatment or prophylaxis of an inflammatory disease and a process of decreasing the expression of one or more of the inflammatory cytokines IFN $-\gamma$ and IL-6 from cells in a mammalian , each comprising administering stressed mammalian blood cells wherein stressor is both oxidative conditions and ultraviolet radiation are under consideration in the instant application.

2. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Canada on 12/05/2000. It is noted, however, that applicant has not filed a copy of the 2,327,631 and 2,327,628 applications as required by 35 U.S.C. 119(b).

3. The disclosure is objected to because of the following informalities: there is no "Brief Description of the Drawings" section in the instant application which describes Figures 1 and 2.

Appropriate correction is required.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> *The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.*

5. Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process of decreasing the expression of one or more of the inflammatory cytokines IFN-γ and IL-6 from cells in mammalian patients comprising administering to the patient an effective amount of stressed mammalian blood cells wherein said blood cells have been extracorporeally subjected to both oxidative conditions and UV radiation does not reasonably provide **enablement** for a method for treatment or prophylaxis of any inflammatory disease, including chronic fatigue syndrome in a patient comprising administering to the patient an effective amount of stressed mammalian blood cells wherein said blood cells have been extracorporeally subjected to both oxidative conditions and UV radiation . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the limited working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The specification only discloses a contact hypersensitivity (CHS) test on Balb/c mice (see Example 1 in particular) and the decrease in the expression levels for cytokines IFN-γ and IL-6 in the lymph tissue of the treated animals (see example 2 in particular) . However, it is noted that there are no data on the change in the ear thickness in treated and control mice.

The specification does not adequately teach how to effectively treat or prophylaxis of any inflammatory disease, including chronic fatigue syndrome in a patient, by administering an effective amount of of stressed mammalian blood cells wherein said blood cells have been extracorporeally subjected to both oxidative conditions and UV radiation. Moreover, no animals models were used to study the effectively of treatment of any inflammatory disease, including chronic fatigue syndrome in a patient, by administering an effective amount of of

stressed mammalian blood cells wherein said blood cells have been extracorporeally subjected to both oxidative conditions and UV radiation. Since there is no animal model studies and data in the specification to show the effectively of treatment or prophylaxis of any inflammatory disease, including chronic fatigue syndrome in a patient comprising administering to the patient an effective amount of stressed mammalian blood cells wherein said blood cells have been extracorporeally subjected to both oxidative conditions and UV radiation it is unpredictable how to correlate a contact hypersensitivity (CHS) test on Balb/c mice and the decrease in the expression levels for cytokines IFN-γ and IL-6 in the lymph tissue of the treated animals with claimed *in vivo* use. Feldman et al (Transplant. Proc. 1998, 30, 4126-4127) teach that "while it is not difficult to study the pathogenesis of animal models of disease, there are multiple constraints on analyses of the pathogenesis of human disease, leading to interesting dilemmas such as how much can we rely on and extrapolate from animal models in disease". In addition, Cochlovius et al (Modern Drug Discovery, 2003, pages 33-38) teach that in contrast to in vitro models, and partly animal-human xenograft systems, tissue cells in vivo seems to express molecules for defense against cellular immune systems as well as against complement. Although these defense mechanisms are still poorly understood, they provide some hints as to why many potential therapeutics perform marvelously in vitro but a fairly high portion of them still fail in vivo. Feldman et al ., further teach that in a chronic immune-driven inflammatory response there are a number of pathways that become engaged and effective therapy in immune inflammatory diseases such as rheumatoid arthritis, will come from therapy aimed at several points in the disease pathway.

Since the method of treatment or prophylaxis of any inflammatory disease, including chronic fatigue syndrome in a patient, by administering an effective amount of stressed mammalian blood cells can be species- and model-dependent (see Van Noort et al. International Review of Cytology, 1998, v.178, pages 127-204, Table III in particular) , it is not clear that reliance on the contact hypersensitivity (CHS) test on Balb/c mice and the decrease in the expression levels for cytokines IFN-γ and IL-6 in the lymph tissue of the treated animals accurately reflects the relative mammal and human efficacy of the claimed therapeutic strategy. The specification does not teach how to extrapolate data obtained from the above discussed studies to the development of effective *in vivo* mammalian including human therapeutic treatment, commensurate in scope with the claimed invention. Therefore, it is not clear that the skilled artisan could predict the efficacy of a method of treatment or prophylaxis of any inflammatory disease, including chronic fatigue syndrome in a patient, by administering an effective amount of stressed mammalian blood cells. Thus in the absence of working examples or detailed guidance in the specification, the intended uses of any pharmaceutical composition comprising stressed mammalian blood cells are fraught with uncertainties.

Moreover, an effective protocol for a method of treatment or prophylaxis of any inflammatory disease, including chronic fatigue syndrome in a patient, is subject to a number of factors which enter the picture beyond simply the administration to the subject an effective amount of stressed mammalian blood cells. The disclosure of a contact hypersensitivity (CHS) test on Balb/c mice and the decrease in the expression levels for cytokines IFN-γ and IL-6 in the lymph tissue

of the treated animals cannot alone support the predictability of a method of treatment or prophylaxis of any inflammatory disease in a patient by administration to the subject an effective amount of stressed mammalian blood cells. Van Noort et al. (International Review of Cytology, 1998) indicate factors that effect immune response such as genetic, environmental and hormonal (Page 176, Paragraph 3). The ability of a host to enhance an immune response will vary depending upon factors such as the condition of the host and burden of disease.

The specification does not provide sufficient teaching as to how it can be assessed that treatment or prophylaxis of any inflammatory disease, including chronic fatigue syndrome was achieved after the administration of a therapeutically effective amount of stressed mammalian blood cells.

Also an issue is whether or not the claimed method would function "for the prophylaxis of any inflammatory disease". The nature of the invention is such that it would require the administration of blood cells that have been extracorporeally subjected to both oxidative conditions and UV radiation that would prevent a mammalian subject from having inflammatory disease. The burden of enabling the prevention of a disease (ie. the need for additional testing) would be greater than that of enabling a treatment due to the need to screen those humans susceptible to such diseases and the difficulty of proof that the administration of stressed blood cells was the agent that acted to prevent the condition. Further, the specification does not provide guidance as to how one skilled in the art would go about screening those patients susceptible to any inflammatory disease, including chronic fatigue syndrome within the scope of the presently claimed invention. Nor is guidance provided as to a specific protocol to be utilized in order to prove the efficacy of the presently claimed compounds in preventing these disease states. Accordingly, undue experimentation is necessary to determine screening and testing protocols to demonstrate the efficacy of the presently claimed invention.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed method of treatment or prophylaxis of any inflammatory disease, including chronic fatigue syndrome comprising administering an effective amount of a therapeutically effective amount of of stressed mammalian blood cells in manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

5.1. Also an issue is that the incorporation of essential material in the specification by reference to Kondo et al. on page 10, line 13 for a contact hypersensitivity test according to approved animal experimentation procedures is improper because an application for a patent when filed may incorporate "essential material" by reference to (1) a United States patent or (2) an allowed U.S. application, see MPEP 608.01(p),. "Essential material" is defined as that which is necessary to (1) support the claims, or (2) for adequate disclosure of the invention (35 U.S.C. 112). "Essential material" may not be incorporated by reference to (1) patents or applications published by foreign countries or regional patent offices, to (2) non-patent publications, to (3) a U.S. patent or application which itself incorporates "essential material" by reference or to (4) a foreign application. See In re Fouche, 169 USPQ 429; 439 F.2d 1237 (CCPA 1971).

Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 2 , 4-6, 8, 10 and 11 are rejected under 35 U.S.C. 102(a) as being anticipated by the WO 00/06703 as is evidenced by Kuby (Immunology, 2-nd ed. 1994, page 573)

The WO ' 703 teaches a method of treating GVHD in a mammalian patient comprises administering to the patient stressed mammalian blood cells (see the entire document Abstract in particular . The WO '703 teaches that stress blood cells have been extracting from the patient an aliquot of blood of volume, contacting the aliquot of blood, extracorporeally subject to at

both oxidative conditions, ultraviolet radiation and heat stress simultaneously. (see overlapping pages 5-6 and 7 in particular). The WO '703 teaches that oxidative environment, such as a mixture of ozone, wherein an ozone content from about 1 to about 100 μg/ml and oxygen bubbled through the blood aliquot, from about 0.5 to 60 min (pages 7 and 9 , in particular). The WO '703 teaches that the temperature stressor is in a range from about 40 to about 55° C (see pages 8 and 11 in particular). The WO '703 teaches that UV stessor is UV-c radiation (see page 8 in particular). Wherein the patient is human and the aliquot of modified mammalian blood is the patient's own blood , of volume from about 0.1-500 ml (page 7, in particular). It is noted that the reference is silent about the fact that disease condition in a patient is mediated by excess inflammatory cytokine production and or abnormal sensitivity of the patient to one or more inflammaroty cytokine, i.e. IL-6 . However, it is clear that both WO ' 703 and applicant administered the same composition, i.e. stressed mammalian blood cells to the same patient to achieve the same results, i.e. treating disease. Even though applicant has proposed the mechanism by which stressed mammalian blood cells alleviates symptoms of an inflammatory disease this does not appear to distinguish the prior art teaching the same methods to achieve the same endresult. Mere recognition of latent properties in the prior art does not render known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145. If the prior art structure is capable of performing the intended use, then it meets the claim. When a claim recites using an old composition or structure (e.g. stressed mammalian blood cells) and the use is directed to a result or property of that composition or structure (treatment of an inflammatory disease) then the claim is anticipated. See MPEP 2112.02. Also, see Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc. 58 USPQ2d 1508 (CA FC 2001); Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

As is evidenced by Kuby , GVHD is an inflammatory disease mediated by excess of inflammatory cytokine production.

Claim 11 in included because the claimed functional limitation would be inherent properties of the claimed method for treating GVHD in a mammalian patient comprises administering to the patient stressed mammalian blood cells. It is clear that both WO ' 703 and applicant administered the same composition, i.e. stressed mammalian blood cells to the same patient thus it would inherently decreasethe expression of one or more of the inflammatory cytokines IFN-γ and IL-6. If the prior art structure is capable of performing the intended use, then it meets the claim. When a claim recites using an old composition or structure (e.g. stressed mammalian blood cells) and the use is directed to a result or property of that composition or structure then the claim is anticipated. See MPEP 2112.02. Also, see Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc. 58 USPQ2d 1508 (CA FC 2001); Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

The reference teaching anticipates the claimed invention.

8. Claims 1, 2 , 4-6, 8, 10 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO 98/07463 or by U.S. Patent No. 5,980,954 .

The WO ' 436 teaches a method of treating an inflammatory disease including inflammatory bowel disease and rheumatoid arthritis in a mammalian patient comprises administering to the patient stressed mammalian blood cells (see the entire document, pages 1, 17, and 23 in particular) . The WO ' 436 teaches that stress blood cells have been extracting from the patient an aliquot of blood of volume, contacting the aliquot of blood, extracorporeally subject to at both oxidative conditions, ultraviolet radiation and heat stress simultaneously. (see overlapping pages 13-14 and 16-17 in particular). The WO ' 436 teaches that oxidative environment, such as a mixture of ozone, wherein an ozone content from about 1.0 to about 100 μg/ml and oxygen bubbled through the blood aliquot, from about 0.5 to 60 min (pages 14-15, in particular). The WO ' 436 teaches that the temperature stressor is in a range from about 40 to about 55° C (see page 14 in particular). The WO ' 436 teaches that UV stessor is UV-c radiation (see page 15 in particular). Wherein the patient is human (page 8, paragraph 3 in particular), and the aliquot of modified mammalian blood is the patient's own blood (page 12, paragraph 4 in particular), of volume from about 0.01-400 ml (pages 8, 13, in particular). It is noted that the reference is silent about the fact that disease condition in a patient is mediated by excess inflammatory cytokine production and or abnormal sensitivity of the patient to one or more inflammaroty cytokine, i.e. IL-6 . However, it is clear that both WO ' 436 and applicant administered the same composition, i.e. stressed mammalian blood cells to the same patient to achieve the same results, i.e. treating disease. Even though applicant has proposed the mechanism by which stressed mammalian blood cells alleviates symptoms of an inflammatory disease this does not appear to distinguish the prior art teaching the same methods to achieve the same endresult. Mere recognition of latent properties in the prior art does not render known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145. If the prior art structure is capable of performing the intended use, then it meets the claim. When a claim recites using an old composition or structure (e.g. stressed mammalian blood cells) and the use is directed to a result or property of that composition or structure (treatment of an inflammatory disease) then the claim is anticipated. See MPEP 2112.02. Also, see Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc. 58 USPQ2d 1508 (CA FC 2001); Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

Similarly, US Patent '954 teaches a method of treating an inflammatory disease including inflammatory bowel disease and rheumatoid arthritis in a mammalian patient comprises

administering to the patient stressed mammalian blood cells (see the entire document, column 1, and overlapping columns 7 –8 in particular) . The US Patent '954 teaches that stress blood cells have been extracting from the patient an aliquot of blood of volume, contacting the aliquot of blood, extracorporeally subject to at both oxidative conditions, ultraviolet radiation and heat stress simultaneously. (see column 6, in particular). The US Patent '954 teaches that oxidative environment, such as a mixture of ozone, wherein an ozone content from about 0.5 to about 100 μg/ml and oxygen bubbled through the blood aliquot, from about 0.5 to 60 min (see overlapping columns 7-8 and Claim 5 in particular). The WO ' 436 teaches that the temperature stressor is in a range from about 40 to about 55° C (see column 7 and claim 4 in particular). The US Patent '954 teaches that UV stessor is UV-c radiation (see column 8 in particular). Wherein the patient is human, and the aliquot of modified mammalian blood is the patient's own blood of volume from about 0.01-400 ml (column 9 and claim 2 in particular). It is noted that the reference is silent about the fact that disease condition in a patient is mediated by excess inflammatory cytokine production and or abnormal sensitivity of the patient to one or more inflammaroty cytokine, i.e. IL-6 . However, it is clear that both US Patent '954 and applicant administered the same composition, i.e. stressed mammalian blood cells to the same patient to achieve the same results, i.e. treating disease. Even though applicant has proposed the mechanism by which stressed mammalian blood cells alleviates symptoms of an inflammatory disease this does not appear to distinguish the prior art teaching the same methods to achieve the same endresult. Mere recognition of latent properties in the prior art does not render known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145. If the prior art structure is capable of performing the intended use, then it meets the claim. When a claim recites using an old composition or structure (e.g. stressed mammalian blood cells) and the use is directed to a result or property of that composition or structure (treatment of an inflammatory disease) then the claim is anticipated. See MPEP 2112.02. Also, see Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc. 58 USPQ2d 1508 (CA FC 2001); Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

Claim 11 in included because the claimed functional limitation would be inherent properties of the claimed method for treating an inflammatory disease in a mammalian patient comprises administering to the patient stressed mammalian blood cells. It is clear that WO ' 436, US Patent' 954 and applicant administered the same composition, i.e. stressed mammalian blood cells to the same patient thus it would inherently decreasethe expression of one or more of the inflammatory cytokines IFN-γ and IL-6. If the prior art structure is capable of performing the intended use, then it meets the claim. When a claim recites using an old composition or structure (e.g. stressed mammalian blood cells) and the use is directed to a result or property of that composition or structure then the claim is anticipated. See MPEP 2112.02. Also, see Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc. 58 USPQ2d 1508 (CA FC 2001); Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52

USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

The references teaching anticipates the claimed invention.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/07463 or U.S. Patent No. 5,980,954 or WO00/06703 each in view of CDC Report (1999).

The teachings of WO 98/07463 , U.S. Patent No. 5,980,954 and WO00/06703 have been discussed, supra.

WO 98/07463 , U.S. Patent No. 5,980,954 or WO00/06703 do not teach treating chronic fatige syndrome.

CDC Report teaches that chronic fatige syndrome is an inflammatory disease mediated by excess inflammatory cytokine production.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of CDS Report to those of WO 98/07463 or U.S. Patent No. 5,980,954 or WO00/06703 to obtain a claimed method for treating chronic fatige syndrome. One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because chronic fatige syndrome is an inflammatory disease mediated by excess inflammatory cytokine production as taught by CDC Report and can be treated by the method for treatment of an inflammatory diseases taught by WO 98/07463 , U.S. Patent No. 5,980,954 or WO00/06703. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would

have been produced by their combination. In re Semaker. 217 USPQ 1, 5 - 6 (Fed. Cir. 1983). See MPEP 2144.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

11. Claims 7 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/07463 , U.S. Patent No. 5,980,954 or WO00/06703.

The teachings of WO 98/07463 , U.S. Patent No. 5,980,954 and WO00/06703 have been discussed, supra.

WO 98/07463 , U.S. Patent No. 5,980,954 or WO00/06703 do not explicitly teach the gaseous mixture that has an ozone content from about 0.1 to about 100 μg/ml and stressed mammalian blood cells of a volume from about 0.1 to about 400 ml.

The claimed blood volume from about 0.1-100 ml is within the reference ranges of 0.01-400 ml taught by WO '463 and US Patent '954 and 0.1 – 500 ml taught by WO'703. The claimed ozone content from about 0.1 to about 100 μg/ml is within the reference ranges of 1.0-100μg/ml, taught by WO'703 and WO'436 and 05-100 μg/ml taught by US Patent '954 . Therefore, the claimed invention is an obvious variation of the reference teachings, absent a showing of unobvious differences. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

12. No claim is allowed.

13. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/272-0841.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michail Belyavskyi, Ph.D.
Patent Examiner
Technology Center 1600
February 23, 2004

Christina Chan

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